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## NOTICE OF ALLOWANCE AND FEE(S) DUE

25885 7590 08/10/2009

ELI LILLY & COMPANY  
PATENT DIVISION  
P.O. BOX 6288  
INDIANAPOLIS, IN 46206-6288

EXAMINER

BLANCHARD, DAVID J

ART UNIT

PAPER NUMBER

1643

DATE MAILED: 08/10/2009

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/555,407

06/08/2007

Dale L. Ludwig

X-18524

7544

TITLE OF INVENTION: FULLY HUMAN ANTIBODIES DIRECTED AGAINST THE HUMAN INSULIN-LIKE GROWTH FACTOR-1 RECEPTOR

APPLN. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	NO	\$1510	\$300	\$0	\$1810	11/10/2009

**THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.**

**THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.**

### HOW TO REPLY TO THIS NOTICE:

#### I. Review the SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

A. If the status is the same, pay the TOTAL FEE(S) DUE shown above.

B. If the status above is to be removed, check box 5b on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and twice the amount of the ISSUE FEE shown above, or

If the SMALL ENTITY is shown as NO:

A. Pay TOTAL FEE(S) DUE shown above, or

B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check box 5a on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and 1/2 the ISSUE FEE shown above.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

**IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.**

# **PART B - FEE(S) TRANSMITTAL**

**Complete and send this form, together with applicable fee(s), to: Mail Mail Stop ISSUE FEE  
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P.O. Box 1450  
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INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

25885 7590 08/10/2009

**ELI LILLY & COMPANY**  
**PATENT DIVISION**  
**P.O. BOX 6288**  
**INDIANAPOLIS, IN 46206-6288**

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

## **Certificate of Mailing or Transmission**

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/555,407 06/08/2007 Dale L. Ludwig X-18524 7544

TITLE OF INVENTION: FULLY HUMAN ANTIBODIES DIRECTED AGAINST THE HUMAN INSULIN-LIKE GROWTH FACTOR-1 RECEPTOR

APPLN. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	NO	\$1510	\$300	\$0	\$1810	11/10/2009

EXAMINER	ART UNIT	CLASS-SUBCLASS
BLANCHARD, DAVID J	1643	530-388150

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

- ☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.
- ☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list

- (1) the names of up to 3 registered patent attorneys or agents OR, alternatively, 1 \_\_\_\_\_
- (2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed. 2 \_\_\_\_\_
- 3 \_\_\_\_\_

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE (B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ☐ Individual ☐ Corporation or other private group entity ☐ Government

4a. The following fee(s) are submitted:

- ☐ Issue Fee
- ☐ Publication Fee (No small entity discount permitted)
- ☐ Advance Order - # of Copies \_\_\_\_\_

4b. Payment of Fee(s); (Please first reapply any previously paid issue fee shown above)

- ☐ A check is enclosed.
- ☐ Payment by credit card. Form PTO-2038 is attached.
- ☐ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment, to Deposit Account Number \_\_\_\_\_ (enclose an extra copy of this form).

5. Change in Entity Status (from status indicated above)

- ☐ a. Applicant claims SMALL ENTITY status. See 37 CFR 1.27. ☐ b. Applicant is no longer claiming SMALL ENTITY status. See 37 CFR 1.27(g)(2).

NOTE: The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

Authorized Signature \_\_\_\_\_

Date \_\_\_\_\_

Typed or printed name \_\_\_\_\_

Registration No. \_\_\_\_\_

This collection of information is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/555,407	06/08/2007	Dale L. Ludwig	X-18524	7544
25885	7590	08/10/2009	EXAMINER	
ELI LILLY & COMPANY PATENT DIVISION P.O. BOX 6288 INDIANAPOLIS, IN 46206-6288			BLANCHARD, DAVID J	
			ART UNIT	PAPER NUMBER
			1643	
DATE MAILED: 08/10/2009				

## Determination of Patent Term Adjustment under 35 U.S.C. 154 (b) (application filed on or after May 29, 2000)

The Patent Term Adjustment to date is 263 day(s). If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the Patent Term Adjustment will be 263 day(s).

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (<http://pair.uspto.gov>).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

<b>Notice of Allowability</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/555,407	LUDWIG, DALE L.	
	<b>Examiner</b>	<b>Art Unit</b>	
	David J. Blanchard	1643	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--**

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 28 May 2009.
2. ☒ The allowed claim(s) is/are 12-14,23-34, 41-49 and 57-60 (renumbered as claims 1-28).
3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  - a) ☐ All    b) ☐ Some\*    c) ☐ None    of the:
    1. ☐ Certified copies of the priority documents have been received.
    2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
    3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\* Certified copies not received: \_\_\_\_\_.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

**THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.**

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
5. ☐ CORRECTED DRAWINGS ( as "replacement sheets") must be submitted.
  - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review ( PTO-948) attached
    - 1) ☐ hereto or 2) ☐ to Paper No./Mail Date \_\_\_\_\_.
  - (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date \_\_\_\_\_.

**Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).**
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

**Attachment(s)**

- |  |   |
|--|---|
| <ol style="list-style-type: none"> <li>1. <input type="checkbox"/> Notice of References Cited (PTO-892)</li> <li>2. <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)</li> <li>3. <input checked="" type="checkbox"/> Information Disclosure Statements (PTO/SB/08),<br/>Paper No./Mail Date <u>See Continuation Sheet</u></li> <li>4. <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit of Biological Material</li> </ol> | <ol style="list-style-type: none"> <li>5. <input type="checkbox"/> Notice of Informal Patent Application</li> <li>6. <input type="checkbox"/> Interview Summary (PTO-413),<br/>Paper No./Mail Date _____.</li> <li>7. <input checked="" type="checkbox"/> Examiner's Amendment/Comment</li> <li>8. <input checked="" type="checkbox"/> Examiner's Statement of Reasons for Allowance</li> <li>9. <input type="checkbox"/> Other _____.</li> </ol> |
|--|---|

/David J Blanchard/  
Primary Examiner, Art Unit 1643

Continuation of Attachment(s) 3. Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date: 12/23/08 (3 pages); 12/23/08 (8 pages).

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### DETAILED ACTION

1. Claims 1-11, 15-22, 35-40 and 50-56 are cancelled.  
Claims 12-14, 23-27 and 30 have been amended.  
Claims 57-60 have been added.
2. Claims 12-14, 23-34, 41-49 and 57-60 are pending.

### *Election/Restrictions*

3. Applicant's election of the Invention of Group I, claims 12-14, 23-33 and newly added claims 57-60 in the reply filed on 28 May 2009 is acknowledged.
4. Claim 34 and 41-49 directed to an allowable product. Pursuant to the procedures set forth in MPEP § 821.04(b), claims 34 and 41-49, directed to the process of making or using the allowable product, previously withdrawn from consideration as a result of a restriction requirement, are hereby rejoined and fully examined for patentability under 37 CFR 1.104. Cancelled claims 19-22 (Group II), 34 and 36-40 (Groups III, IV and V), directed to the invention(s) of nucleic acids, vectors and host cells encoding a human antibody or fragment thereof that binds IGF-IR (Group I) and methods of treating acromegaly, retinal neovascularization and psoriasis comprising administering a human antibody or fragment thereof that binds IGF-IR (Groups III, IV and V, respectively) have NOT been rejoined.

Because a claimed invention previously withdrawn from consideration under 37 CFR 1.142 has been rejoined, **the restriction requirement among groups I and VI as set forth in the Office action mailed on 28 April 2009 is hereby WITHDRAWN. For clarity, it is noted that the restriction requirement among groups II, III, IV and V as set forth in the Office action mailed on 28 April 2009 is MAINTAINED.** In view of the withdrawal of the restriction requirement as to the rejoined inventions, applicant(s) are advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, a claim that is allowable in the present application, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Once the restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. See *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

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***Information Disclosure Statement***

5. The Information Disclosure Statement (IDS) filed 23 December 2008 (3 pages) and 23 December 2008 (twelve pages) have been considered by the Examiner. A signed and initialed copy of each IDS is included with the instant Office Action.

**Examiner's Amendment**

6. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Sanjay M. Jivraj on 29 July 2009

**The claims are amended as follows:**

12. (Currently Amended) An isolated human antibody or fragment thereof, which specifically binds to insulin-like growth factor-I receptor (IGF-IR) comprising complementarity-determining ~~region (CDR)~~ regions (CDRs) having the amino acid sequence SEQ ID NO:14 at V<sub>H</sub>CDR1, SEQ ID NO:16 at V<sub>H</sub>CDR2, SEQ ID NO:18 at V<sub>H</sub>CDR3, SEQ ID NO:20 or 26 at V<sub>L</sub>CDR1, SEQ ID NO:22 or 28 at V<sub>L</sub>CDR2, and SEQ ID NO:24 or 30 at V<sub>L</sub>CDR3.

13. (Currently Amended) The antibody or ~~antigen-binding~~ fragment thereof of Claim 12, which comprises SEQ ID NO:14 at V<sub>H</sub>CDR1, SEQ ID NO:16 at V<sub>H</sub>CDR2, SEQ ID NO:18 at V<sub>H</sub>CDR3, SEQ ID NO:20 at V<sub>L</sub>CDR1, SEQ ID NO:22 at V<sub>L</sub>CDR2, and SEQ ID NO:24 at V<sub>L</sub>CDR3.

14. (Currently Amended) The antibody or ~~antigen-binding~~ fragment thereof of Claim 12, which comprises SEQ ID NO:14 at V<sub>H</sub>CDR1, SEQ ID NO:16 at V<sub>H</sub>CDR2, SEQ ID NO:18 at V<sub>H</sub>CDR3, SEQ ID NO:26 at V<sub>L</sub>CDR1, SEQ ID NO:28 at V<sub>L</sub>CDR2, and SEQ ID NO:30 at V<sub>L</sub>CDR3.

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Claims 15-22 (Cancelled)

23. (Currently Amended) A pharmaceutical composition comprising the antibody or ~~antibody~~ fragment thereof of Claim 12 and a pharmaceutically acceptable carrier.

24. (Currently Amended) A conjugate comprising the antibody or ~~antibody~~ fragment thereof of Claim 12 linked to a cytotoxic agent.

25. (Currently Amended) A conjugate comprising the antibody or ~~antibody~~ fragment thereof of Claim 12 linked to a label.

26. (Currently Amended) A therapeutic composition effective to inhibit growth of human tumor cells that express IGF-IR, which composition comprises the antibody or ~~antigen-binding~~ fragment thereof of Claim 12.

27. (Currently Amended) The therapeutic composition of Claim 26, which further comprises an antineoplastic agent.

28. (Original) The therapeutic composition of Claim 27, wherein the anti-neoplastic agent is an inhibitor of topoisomerase I or topoisomerase II.

29. (Original) The therapeutic composition of Claim 27, wherein the anti-neoplastic agent is selected from the group consisting of irinotecan, camptothecin, and etoposide.

30. (Currently Amended) A therapeutic composition effective to promote regression of human tumors that express IGF-IR, which composition comprises the antibody or ~~antibody~~ fragment thereof of Claim 12.



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31. (Original) The therapeutic composition of Claim 30, which further comprises an antineoplastic agent.

32. (Original) The therapeutic composition of Claim 31, wherein the anti-neoplastic agent is an inhibitor of topoisomerase I or topoisomerase II.

33. (Currently Amended) The therapeutic composition of Claim 31, wherein the anti-neoplastic agent is selected from the group consisting of irinotecan, camptothecin, ~~[[or]]~~ and etoposide.

34. (Currently Amended) A method of neutralizing the activation of ~~[[IGF-LR]]~~ IGF-IR, which comprises administering to a mammal an effective amount of the antibody or ~~antibody~~ fragment thereof of Claim 12

Claims 35-40 (Cancelled)

41. (Currently Amended) A method of reducing tumor growth which comprises administering to a mammal an effective amount of the antibody or ~~antibody~~ fragment thereof of Claim 12.

42. (Original) The method of Claim 41, which further comprises administering an effective amount of an anti-neoplastic agent.

43. (Original) The method of Claim 42, wherein the anti-neoplastic agent is an inhibitor of topoisomerase I or topoisomerase II.

44. (Original) The method of Claim 42, wherein the anti-neoplastic agent is selected from the group consisting of irinotecan, camptothecin, and etoposide.

45. (Currently Amended) A method of promoting tumor regression which comprises administering to a mammal an effective amount of the antibody or ~~antibody~~ fragment thereof of

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Claim 12.

46. (Original) The method of Claim 45, which further comprises administering an effective amount of an anti-neoplastic agent.

47. (Original) The method of Claim 46, wherein the anti-neoplastic agent is an inhibitor of topoisomerase I or topoisomerase II.

48. (Original) The method of Claim 46, wherein the anti-neoplastic agent is selected from the group consisting of irinotecan, camptothecin, and etoposide.

49. (Original) The method of any one of Claims 41 to 48, wherein the tumor is a breast tumor, colorectal tumor, pancreatic tumor, ovarian tumor, lung tumor, prostate tumor, bone or soft tissue sarcoma or myeloma.

Claims 50-56 (Cancelled)

57. (Currently Amended) An ~~antibody~~ isolated human antibody or fragment thereof comprising ~~represented by~~ of SEQ ID NO:2 and ~~represented by~~ of SEQ ID NO:6.

58. (Currently Amended) An ~~antibody~~ isolated human antibody or fragment thereof comprising ~~represented by~~ of SEQ ID NO:2 and ~~represented by~~ of SEQ ID NO:10.

59. (Currently Amended) The antibody of ~~Claims 57-58~~ Claims 57 or 58, wherein said antibody has an IgG1 isotype.

60. (Currently Amended) A pharmaceutical composition comprising the antibody of ~~Claims 57-59~~ Claims 57 or 58 and a pharmaceutically acceptable carrier.

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**Amendments to the specification**

On page 1, please delete paragraph [0001] and replace it with the following paragraph:

[0001] This application claims ~~the benefit of United States Provisional Application 60/467,177, filed May 1, 2003~~ priority of and is a U.S. national phase application of PCT/US2004/013852, filed May 3, 2004, which claims priority of U.S. Provisional Application No. 60/467,177, filed May 1, 2003.

Please Amend Paragraphs 15-26 on pages 6 and 7 as follows;

[0015] Figure 1 depicts the nucleotide sequence of the 2F8 heavy chain variable domain (SEQ ID NO:1).

[0016] Figure 2 depicts the amino acid sequence of the 2F8 heavy chain variable domain. CDRs are in bold and underlined (SEQ ID NO:2).

[0017] Figure 3 depicts the nucleotide sequence of the complete 2F8 heavy chain (underline: secretory signal sequence; italics: IgG1 constant region) (SEQ ID NO:3).

[0018] Figure 4 depicts the amino acid sequence of the complete 2F8 heavy chain (underline: secretory signal sequence; bold: CDRs; italics: IgG1 constant region) (SEQ ID NO:4).

[0019] Figure 5 depicts the nucleotide sequence of the 2F8 light chain variable domain (SEQ ID NO:5).

[0020] Figure 6 depicts the amino acid sequence of the 2F8 light chain variable domain. CDRs are in bold and underlined (SEQ ID NO:6).

[0021] Figure 7 depicts the nucleotide sequence of the complete 2F8 light chain (underline: secretory signal sequence; italics: IgG1 constant region) (SEQ ID NO:7).

[0022] Figure 8 depicts the amino acid sequence of the complete 2F8 light chain (underline: secretory signal sequence; bold: CDRs; italics: IgG1 constant region) (SEQ ID NO:8).

[0023] Figure 9 depicts the nucleotide sequence of the A12 light chain variable domain (SEQ ID NO:9).

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[0024] Figure 10 depicts the amino acid sequence of the A12 light chain variable domain. CDRs are in bold and underlined (SEQ ID NO:10).

[0025] Fig. 11 depicts the nucleotide sequence of the complete A12 light chain (underline: secretory signal sequence; italics: IgG1 constant region) (SEQ ID NO:11).

[0026] Figure 12 depicts the amino acid sequence of the complete A12 light chain (underline: secretory signal sequence; bold: CDRs; italics: IgG1 constant region) (SEQ ID NO:12).

Please Amend Paragraph 81 on page 18 as follows;

[0081] In another embodiment, the present antibodies, or fragments thereof, can have a heavy chain variable region of ~~SEQ ID NO:1~~ SEQ ID NO: 2 and/or a light chain variable region selected from ~~SEQ ID NO:5 or SEQ ID NO:6~~ SEQ ID NO:6 or SEQ ID NO:10. IMC-A12 is a particularly preferred antibody of the present invention. This antibody has human V<sub>H</sub> and V<sub>L</sub> framework regions (FWs) as well as CDRs. The V<sub>H</sub> variable domain of IMC-A12 (~~SEQ ID NO:1~~ SEQ ID NO:2) has three CDRs corresponding to SEQ ID NOS:14, 16, and 18 and the V<sub>L</sub> domain (~~SEQ ID NO:5~~ SEQ ID NO:10) has three CDRs corresponding to ~~SEQ ID NOS:20, 22, and 24~~ SEQ ID NOS:26, 28, and 30. IMC-2F8 is another preferred antibody of the present invention. This antibody also has human V<sub>H</sub> and V<sub>L</sub> framework regions (FWs) and CDRs. The V<sub>H</sub> variable domain of IMC-2F8 is identical to the V<sub>H</sub> variable domain of IMCA12. The V<sub>L</sub> domain of IMC-2F8 (~~SEQ ID NO:9~~ SEQ ID NO:6) has three CDRs corresponding to ~~SEQ ID NOS:26, 28, and 30~~ SEQ ID NOS:20, 22, and 24.

#### **Examiner's Statement of Reasons for Allowance**

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

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Claims 12-14, 23-33 and 57-60 are free of the prior art. The prior art does not teach or fairly suggest an isolated human antibody or fragment thereof comprising the recited heavy and light chain CDR sequences or an antibody comprising the heavy chain variable domain of SEQ ID NO:2 and the light chain variable domain of SEQ ID NO:6 or 10.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832.

The official fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/David J. Blanchard/  
Primary Examiner, A.U. 1643